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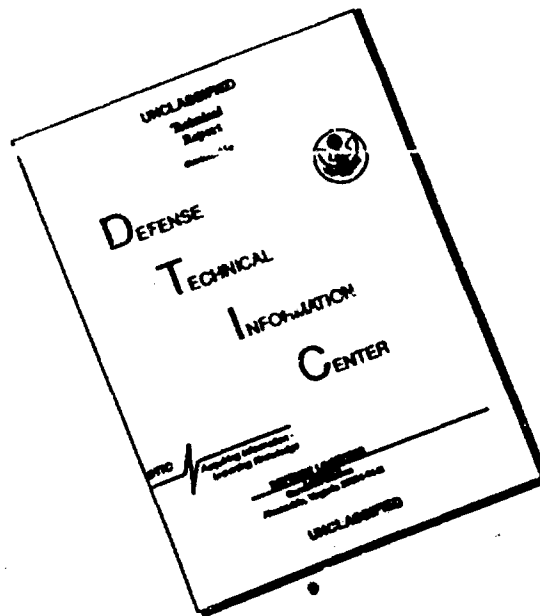
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ON THE EXISTENCE OF TWO TYPES OF ANTIBODIES TO DNA

[Following is the translation of an article by A. M. Poverenny and M. I. Levi, Institute of Medical Radiology, AMN USSR, Obninsk, and the Rostov Medical Institute, published in the Russian-language periodical Voprosy Meditsinskoy Khimii (Problems of Medical Chemistry) Vol XI, No 2, 1965, pages 95-97. It was submitted on 20 Oct 1964. Translation performed by Sp/7 Charles T. Ostertag, Jr.]

During various investigations [1--3], in which a number of immunological methods were used, it was possible to detect antibodies to DNA in the sera from patients with systemic lupus erythematosus (SLE).

It is known that the reaction of passive hemagglutination (PHAR) is one of the most simple and sensitive of immunological methods.

Earlier various authors [3, 4] made unsuccessful attempts to use this reaction for the detection of antibodies to DNA. Having found conditions which permit the adsorption of DNA on the surface of erythrocytes, we used the PHAR for the detection of antibodies to DNA and for their investigation in healthy and sick persons and in certain experimental animals.

The conditions for setting up the PHAR, the passive hemagglutination Inhibition Reaction (PHAIR), and the antibody neutralization reaction (ANR) were described in detail by us earlier /5/. In the ANR and the PHAIR we used DNA of a bacterial origin /6/. During the mass investigation of sera we used erythrocytes, on the surface of which was adsorbed DNA isolated from chicken erythrocytes /5/. In the ANR we used highly polymerized RNA, isolated from rabbit liver by the method of phenol deproteinization /7/.

The PHAIR and ANR were set up with sera in which the PHAR was positive. In these reactions we used native DNA (maximum concentration of 10 g/ml), single-stranded DNA (preparations of DNA, heated at 100° in the presence of formaldehyde), DNA treated with desoxyribonuclease under optimum conditions, native RNA (250 g/ml), RNA heated in the presence of formaldehyde, and RNA subjected to the action of ribonuclease under optimum conditions.

With the help of the PHAR we investigated the sera of a large number of healthy persons and patients with SLE, leprosy, and tuberculous bronchadenitis. In addition to this we investigated the sera of various experimental animals. The results are presented in table 1.

As can be seen from the table, a large part of the sera reacted positively in the PHAR. It was shown that in the ANR for the neutralization of a volume of serum, containing 1--2 serumal units /5/, it was necessary to have 0.003-0.012 g of single-stranded DNA. They could not be neutralized with considerably greater quantities (up to 40 g) of native DNA, DNA, subjected to the action of desoxyribonuclease, and by various preparations of RNA; native heated in the presence of formaldehyde or treated with ribonuclease. The results testify that in the serum of the majority of healthy persons, and also in many of the experimental animals, there are present antibodies which interact with single-stranded DNA.

In the sera from patients with SLE, leprosy and bronchoadenitis in titers of 1:40 and greater, a statistically reliable higher titer is observed in the antibodies to DNA in comparison with healthy persons.

During the investigations of guinea pigs of various age and weight (the age is correlated with the weight) it was detected that the quantity of antibodies to single-stranded DNA increases with age. These data are presented in table 2.

These data are of interest in connection with the fact that recent reports appeared on the detection of the constant presence of an anti-nuclear factor in the serum of one of the strains of mice. It appears for the first time in 10-week old animals and is present almost constantly in 40-week old animals /8/.

There is special interest in the data obtained during the investigation of sera from patients with SLE. We reported earlier that in the ANR investigations of DNA preparations with a various nucleotide composition ($A + T/G + C = 0.4--2$), it was not possible to detect differences in the capability to neutralize antibodies present in the sera of SLE patients /5/. However, differences were revealed in the ANR when native and single-stranded DNA were used. It turned out that the neutralization of 10 sera from SLE patients could occur only when single-stranded DNA was used (just as in other cases when we detected a positive response in the PHAR). In addition to this, we detected 3 sera, the antibodies of which could be neutralized both by native and single-stranded DNA. For the neutralization of antibodies in these cases, it required a lesser amount of native DNA (0.01; 0.015; 0.04 g) than of single-stranded (0.06; 0.03; 0.16 g).

It is important to note that in the course of our investigations we observed 3 cases with a fatal outcome in SLE patients. These were those patients, the antibodies of which interacted with native and single-stranded molecules of DNA. There is considerable interest in data concerning a change of antibodies in one patient with SLE. While during the first period of observation the antibodies present in her sera

were neutralized only by single-stranded molecules, after 1½ years their binding required 0.12 g of native DNA and 0.04 g of denatured.

The data cited testify to the fact that in the sera of patients with SLE, it is possible that at least 2 types of antibodies to DNA are present: Antibodies interacting only with single-stranded molecules of DNA, and antibodies combining with both native and single-stranded preparations of DNA. Antibodies of the first type are encountered sufficiently often in healthy persons and various experimental animals. Their quantity, as was already noted, increases during certain illnesses: Leprosy, tuberculous bronchoadenitis. We observed a considerable increase in the quantity of antibodies to single-stranded DNA during scrofuloderma and during banal lymphadenitis accompanied by suppuration of the lymph node. However, due to an insufficient amount of material we cannot make a final conclusion. The impression is created that one of the reasons for the appearance of antibodies to DNA may be inflammatory processes accompanied by suppuration in the lymphatic apparatus.

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Table 1

Antibodies to DNA in the blood serum from healthy and sick persons and experimental animals

Investigated	Number investigated	Activity of sera in the PHAR based on titers						
		0*	1:10	1:20	1:40	1:80	1:160	1:320
Healthy persons . . .	587	263	77	132	82	26	7	-
Patients with:								
SLE	14	-	-	-	-	2	3	2
Leprosy	19	1	1	3	5	5	2	1
Bronchoadenitis . .	13	1	2	-	3	3	2	2
Guinea pigs	130	27	7	21	35	26	11	3
White rats	65	20	-	-	1	2	15	27
Hamster	52	32	4	3	3	-	-	-
Rabbits	33	14	5	12	2	-	-	-
White mice	4	1	1	1	-	-	-	1

* This column includes sera which in dilutions of 1:10 were negative

Table 2

Dependency between the weight of the guinea pigs and the titer of antibodies to single-stranded DNA.

Weight of animals (in grams)	A-ctivity of sera						
	0*	1:10	1:20	1:40	1:80	1:160	1:320
	Number of animals						
230	11	11	4	6	9	1	-
650	-	-	1	1	1	7	-

* This column includes sera, negative in a titer of 1:10.